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Bioterrorism Preparedness: People, Tools, and Systems for Detecting and Responding to a Bioterrorist Attack

A Summary of Continuing Scientific Research Efforts at The Institute of Environmental and Human Health, Texas Tech University

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Overview and History of The Institute of Environmental and Human Health:

In 1997, Texas Tech University and Texas Tech University Health Sciences Center established, as a joint venture, The Institute of Environmental and Human Health (TIEHH) to bridge their ability to assess the impacts of toxic chemicals on the environment and on human beings. This initiative employs a medical school and health sciences center interfaced with a comprehensive university, including the Texas Tech University School of Law, and represents an opportunity to address environmental and human health issues from a multi-disciplinary perspective. Research members have been recruited based on experience in the field of environmental toxicology, as well as the diversity of their research. Dr. Ronald J. Kendall, a prominent leader in the international toxicology community, was hired as the founding director of TIEHH to direct this team and recruit the best scientists and personnel in this field.

TIEHH research assesses human exposure to chemicals in the environment associated with symptomologies that can be determined to enhance and standardize the diagnostic process. TIEHH builds upon analytical methods of elements from human exposure to enhance quantitation of chemicals in association with environmental exposures. TIEHH also builds upon population-based epidemiological studies, including both humans and wildlife, to begin to better define the "Canary in the Coal Mine" concept from a more quantitative and rigorous scientific basis. TIEHH is developing new innovative approaches to assess human health consequences in the environment.

In a very short time, experts at TIEHH have created a one-of-a-kind program working to find answers to real-world issues. Incorporating a multidisciplinary group of scientists, scholars, business leaders and government agencies, TIEHH personnel have assembled the best minds in the country to research environmental issues and provide solutions. Located in Lubbock, Texas, on the former Reese Air Force Base which is now Reese Technology Center, TIEHH occupies six buildings and more than 150,000 sq. ft. Over $15 million was invested through several state and federal agencies, as well as support from Texas Tech, for the building and laboratory renovation and capital improvements. This includes over $3 million for the renovation of facilities and purchase of a high performance computing system and virtual reality theatre equipment that is housed in TIEHH.

As of Fiscal Year 2002-2003, TIEHH has facilitated approximately $50 million in grants and contracts awarded to Texas Tech University since TIEHH's establishment in 1997. Active grants facilitated by TIEHH core and research faculty and collaborators include the following sponsors: Strategic Environmental Research and Development Program, U.S. Army Soldier and Biological Chemical Command, Environmental Protection Agency, National Institute of Health, U.S. Department of Agriculture, National Institute of Environmental Health Sciences, National Science Foundation, and U.S. Army Corps of Engineers.

Admiral Elmo R. Zumwalt, Jr. National Program for Countermeasures to Biological and Chemical Threats:

For almost five years The Institute of Environmental and Human Health at Texas Tech University has been the home of the Admiral Elmo R. Zumwalt, Jr. National Program for Countermeasures to Biological and Chemical Threats (Zumwalt Program), which is a multidisciplinary research, education, and service consortium composed of more than 60 research scientists. The Zumwalt Program was formally established in 1999 with the primary mission of defining, investigating, mitigating, and furthering the understanding and ability of operational military forces to prevent the threats associated with biological and chemical weapons. Inspired by the leadership of the late Admiral Elmo R. Zumwalt, Jr., the former Commander of Naval Operations during the Vietnam War, Dr. Ronald Kendall, Director of TIEHH, took the steps necessary to begin a countermeasures research program at Texas Tech University (TTU). He and others judiciously selected a team of multidisciplinary intellectual and technological experts from the Texas Tech University System and charged them with developing effective countermeasure strategies that would improve the Nation's understanding of biological and chemical weapons. By late 1999, these efforts culminated in a large research consortium that submitted a white paper designed to meet the critical needs of the National Research Council. A short time later the U. S. Congress appropriated funding to the Texas Tech University System, the University of Texas at Austin, and the University of South Florida to support research and technology development, training and education for countermeasures to biological and chemical threats, the Zumwalt Program received funding from the U.S. Army Soldier Biological and Chemical Command (SBCCOM) to establish and implement the research initiative (in October 2003 the SBCCOM was reorganized and renamed the U.S. Army Research, Development and Engineering Command (RDECOM)).

The administrative and support functions to facilitate all elements of the Zumwalt Program are headquartered at TIEHH. Once established and initiated, the Zumwalt Program used SBCCOM funding to expand and branch out to recruit scientists and conduct research in more than 12 different departments within the TTU System. Each research project is peer-reviewed to insure it complements the overall Zumwalt Program and SBCCOM/RDECOM mission, which is to develop, acquire, and sustain soldier support and nuclear, biological, and chemical defense technology, systems, and services. The start-up funding enabled individual scientists within the Zumwalt Program to bring their individual expertise and laboratory resources to bear on the threats of biological and chemical weapons and threat agents. The Zumwalt Program at Texas Tech is part of the National Consortium for Countermeasures to Biological and Chemical Threats (National Consortium), which represents efforts contributed from Arkansas State University, Florida Atlantic University, Kansas State University, Oklahoma State University, University of Central Florida, University of Kansas, University of South Florida, University of Texas System, and the Texas Tech University System.

Vision, Objectives, and Collaborations: Created by the best and brightest of the TTU System, the Zumwalt Program envisioned that its efforts would result in a long-term and much-needed biological and chemical weapon and threat agent research program. Initially envisioned as a means for creating professional jobs for West Texans, this program is now positioned to significantly contribute to improving national security. In an effort to minimize start-up costs and maximize research, the Zumwalt Program is permanently housed at TIEHH where an Administrative Support Team has been continually utilized to ensure solutions were provided to the problems associated with biological and chemical threat agents. The initial prime objective of the Zumwalt Program was to develop and lead collaborative efforts with other academic institutions involved in countermeasures research. This objective was achieved. In fact, after three years, intercollegiate collaborations continue to be developed with other academic institutions which now include the University of South Florida's Center for Biological Defense, the University of Texas, Oklahoma State University, the University of Kansas, Texas A&M University, and the Johns Hopkins Applied Physics Laboratory. Evidence of these successful collaborations was displayed when Texas Tech hosted the 2003 Consortium of Biological Defense Research Meeting (CBDR) where more than 80 scientists presented over 30 technical presentations concerning the detection, mitigation, and prevention of biological and chemical weapon and threat agents.

Specific Questions Addressed:

1. *What tools and systems is the Institute of Environmental and Human Health (TIEHH) working on to detect and respond to a bioterrorist attack? What organizations provide the funding to support this research and development? How are the resulting technologies transitioned to users?*

The Zumwalt Program continues its focus of coordinating and integrating all expert, multidisciplinary intellectual and technological resources available to design, develop and field effective and efficient strategies, devices and therapeutics to combat biological and chemical weapons of terrorism or of mass destruction. The Zumwalt Program team at TTU is composed of more than 60 research scientists collaborating to meet our mission. The focus of our endeavors remains the leveraging of previous successes, advancement and continuity of our multidisciplinary team to exploit all identified and novel opportunities to meet the nation's biological and chemical threat countermeasures research and development needs as identified by the Institute of Medicine's National Research Council:

- Pre-incident communications and intelligence
- Personal protective equipment
- Detection and measurement of chemical and biological agents
- Recognizing covert exposure
- Mass-casualty decontamination and triage procedures
- Availability, safety, and efficacy of drugs, vaccines and other therapeutics
- Computer-related tools for training and operations

Specific ongoing research efforts being conducted by scientists under the auspices of the Zumwalt Program to protect against and respond to potential bioterrorism incidents, are focused upon four areas, including: (1) The modeling, simulation and visualization of how biological threat agents may disperse through an environment following release. (2) Developing and refining technologies for agent detection, remediation and therapeutic intervention strategies. (3) Developing new and assessing existing technologies to create sensors and personal protective devices for biological and chemical threats. And (4), the design and development of technologies to protect buildings and the environment from biological and chemical weapons. During fiscal year 2003, the outstanding team of research scientists working as part of the Zumwalt Program successfully completed research in these four focus areas, as detailed below:

Focus Area I: Modeling, Simulation and Visualization

- ***Modeling and Simulation of Scavenging Degradation and Deposition of Chemical and Biological Contaminants in the Urban Environment* –** While most modeling and simulation projects have concentrated efforts upon determining and predicting the dispersive characteristics of chemical and biological agent plumes or clouds around buildings in an urban environment, this project seeks to understand the effects that vegetative canopy, scavenging contaminants, degradation of the chemical and biological agents as they interact with ambient radiation and urban pollutants or deposition and potential resuspension or re-evaporation of contaminants have on plume or cloud dispersion within the urban environment. Most currently-used models do not account for these post-release factors that are believed to profoundly affect the dispersion and concentration patterns, possibly leading to large errors in simulation accuracy. A primary focus of this program is to formulate and test boundary conditions that account for these post-release phenomena for codes that predict contaminant transport and dispersion. An understanding of the vegetative canopy flow is fundamental to improving the accuracy and ability to characterize urban dispersion patterns, including the street-level patterns. For this reason, investigators have gone to great lengths to study and understand data unique to vegetative canopies, including tree type, leaf size, and tree-stand arrangement. Models have been created that show particle movement and deflection around vegetative canopies and are proving to be very useful for estimating the risk that response teams may face when attempting to rescue casualties or entering and cleaning-up contaminated areas. Collaboration between TIEHH and the Atmospheric Sciences Group has lead to significant leveraging opportunities with the Governor of Texas Homeland Security Office and Division of Emergency Management of the Texas Department of Public Safety.

- ***Modeling Airborne Transport of Hazards Using Advanced Atmospheric Monitoring Systems and Numerical Techniques* –** The objective of this project is to evaluate the capabilities and limitations of mesoscale (10-100 km range) atmospheric models for chemical and biological agent airborne transport prediction. It is critically important to understand how biological and chemical agents are physically dispersed and transported in the atmosphere. Accurate simulation or near real-time assessments of chemical and biological threats depend upon accurate interpretations and forecasting of atmospheric conditions. Work conducted during 2002 has allowed investigators to develop and deploy portable field meteorological data sensor and recording platforms. Optimizing and enhancing the meteorological data handling of current DoD models will allow for accurate simulations of potential scenarios in advance of chemical/biological attacks, the determination of where and when specific populations or targets would be at risk given specific criteria, determination points of release and environmental conditions, and allow the tracing back of the trajectory of detected airborne agents in order to locate and neutralize its release point. These platforms were tested under severe weather events, included hurricane Lilli and tropical cyclones Fay and Isadore. The high-resolution atmospheric data gathered during these storm events can be used to better predict biological and chemical agent dispersion in the atmosphere. Additionally, significant leverage opportunities have resulted with the Texas Division of Emergency Management, as well as the testing of these capabilities during a training event held in the Houston Shipping Channel. Future leverage opportunities appear likely with atmospheric research groups in Oklahoma and New Mexico.

- ***Determining Spread Pattern of Microbial Food Toxins in Agricultural Systems –*** Agriculture-related terrorism is a real and present threat to our country's food supply and economic stability. The primary objective of this project is to determine and follow the spread pattern of ricin/ricinine from the point of contamination on the soil surface to its ultimate detoxification/ degradation. Investigators have identified and characterized a ricin-contaminated test-site within an existing field. This field has been used to grow castor beans for many years and investigators have detected a significant ricin gradient within the soil. Innovative techniques have been developed and implemented to qualify and quantify ricin levels in the soil. Abiotic factors including soil types, mineralogy, pH, salinity, moisture as well as biotic factors, fungi and bacteria, are primary factors in the capacity of the soil to sequester or mitigate the ricin/ricinine. From data resulting from studies of spread patterns during 2001, investigators are focusing on determining or developing new ways to mitigate the spread of this dangerous toxin. Recent discoveries of direct links between the al-Qaida network and the Iraqi military, and plans to utilize ricin on the battlefield, heighten the need to find means to mitigate the toxin.

Focus Area II: Agent Detection, Remediation and Therapeutic Intervention Strategies

- ***Cellular Transduction Mechanisms Involved in Latent Neurodegeneration of Motor And Cognitive Central Nervous System Sites –*** Chemical warfare agents, particularly organophosphate-based agents and biological toxins pose a significant threat to both military and civilian personnel and have the potential to both acutely and chronically impact the human nervous system. Long term consequences associated with intermittent or continued exposure to these toxicants appear to arise from excessive levels of glutamate and activation of AMPA-preferring glutamate receptors. There is some evidence to suggest that syndromes such as the Gulf War Syndrome experienced by Desert Storm veterans is the latent result of chemical exposure. Broadly, there needs to be a scientific basis for understanding and preventing acute and delayed neuronal cell death. Specifically this study was initiated to determine whether AMPA-receptor-induced dark cell degeneration (DCD) in Purkinje neurons is associated with the translocation of Bax, cytochrome C release from the mitochondria and activation of representative initiator and executor caspases that include caspase-9, caspase-3, and caspase-7. Investigators have concluded that stress-activated kinases are instrumental in mediating AMPA-induced DCD, and allow for the assumption that AMPA-induced toxicity is pharmacologically ameliorated with MAP antagonists. Developing therapies to control cell death in a programmed manner may prove beneficial in mitigating long-term effects of exposure to various chemical agents.

- ***The Isolation and Characterization of Combinatorial Peptides for the Detection and Neutralization of Bioagents* -** Isolation and characterization of high affinity peptide ligands is a useful and possibly a more economical means for detecting and neutralizing biological warfare agents. Using principles of combinatorial peptide chemistry along with affinity maturation of phage display peptides, this project will continue to investigate peptide ligands with high binding affinity for ricin, cholera, tetanus, and shiga toxins. During 2002, investigators identified peptide display phages with binding affinity for ricin and cholera toxin. These discoveries were critical in gaining the ability to detect ricin and cholera toxins in very low concentrations. Additionally, a capillary bio-panning apparatus was developed that can be used for automated biopanning of phage display libraries.

- ***Microsystems for Detecting Liquid and Gaseous Hazards* –** Fluorescent Spectroscopy is used to identify and quantify trace contaminants by looking for their characteristic optical "fingerprint". This spectrophotometric sensing approach is a cornerstone of analytical chemistry and increasingly finds applications for monitoring biological and chemical agents. This project is focused on the development of enabling technologies needed for next generation sensors and integrating optic spectroscopic techniques into a compact biological and chemical agent warning device. Investigators have fabricated a hybrid mini-fluorescence/absorption spectroscopy system, the materials for a UV light emitting diode, microfluidics, and an analysis and deconvolution system. Liquid core waveguide technology has also been used successfully to improve this project. The hybrid-integrated mini-fluorescence/absorption system incorporates mostly small and discrete parts and is under computer control that uses a laptop for data output.

- ***Combinative Toxicity of Biotoxin Mixtures* –** Biotoxins are naturally occurring toxic agents produced by bacteria, cyanobacteria, fungi and some species of plants or marine fish and are etiological agents for a variety of animal and human toxicoses. Several biotoxins such as aflatoxin, T-2 toxin, anatoxin, botulinum toxin, microcystins, ricin, saxitoxin, staphylococcal enterotoxin, and tetrodotoxin are known to be potential biological weapons. Synergistic and potentiation effects of biotoxin mixtures may enhance casualties and cause long-term effects in affected human populations. The objective of this study is to investigate the mechanisms of combinative toxic effects on animals and humans to facilitate the development of protective strategies against potential use of these mixtures as biological warfare threat agents or terrorist attack agents. Investigators tested the acute toxicity of four biotoxins, including aflatoxin B1, T-2 toxin, microcystin-LR and fumonisin, in rats and fish. The respective toxic index for these toxins was developed. Additionally, antibody-based immunoaffinity methods, enzyme-linked immunosorbent assays, and radioimmunoassay were established for measuring these biotoxins in the laboratory as well as for a small number of environmental samples. Investigators also optimized the experimental conditions, including parameters such as cell numbers, incubation times, substrate concentrations, and biotoxin solubilities. Significant leverage opportunities have already been demonstrated with cancer research centers in China. Future research collaborations include environmental research in Vietnam.

- ***Counter-Terrorism Measures to Combat Yersinia pestis with Selenium Pharmaceuticals* –** The primary objective of this research is to produce selenium-labeled peptides and phage (bacterial viruses) that can selectively bind to the surface of pathogenic bacteria and inactivate them through the generation of superoxide radicals on their surface. Initial results have demonstrated that selenium could be covalently bonded to organic molecules and would continue to retain its ability to kill bacteria. Additionally, investigators identified specific peptide sequences for high specificity and affinity for *Yersinia pestis*. Some of these sequences have been synthesized and labeled with selenium display phages. Most importantly, investigators have demonstrated that using the selenium-labeled phage, bacteria can now be killed in 30 minutes, as opposed to 36 hours. Plans have been initiated with members of the DoD to test the *in vivo* efficacy of these phage on *Y. pestis*.

Focus Area III: Sensors and Personal Protective Devices

- ***Development of Lightweight Nonwoven Protective Clothing for Chemical and Biological Warfare Protection* -** Non-woven substrates are a novel and promising approach for use in the development of protective clothing substrates because they are lightweight, breathable, and comfortable. The purpose of this project is to use state-of-the-art non-woven technology to produce fabrics capable of providing chemical protection. Researchers have produced non-woven substrates with high tensile strength and have incorporated an activated carbon layer that is thought to provide a significant amount of chemical absorbency. Additionally, the research team was able to use thermal bonding technology to incorporate chemical sensor prototypes into wall coverings. This project has generated substantial scientific, industry and media attention and has been featured in local and regional coverage. Results from this project has led to the filing of two patents and has significantly increased public and industry awareness for TIEHH, TTU, and TTU's Office of Technology Transfer and Intellectual Property.

- ***Development of a Fluid-Based Fluorescent Bioaerosol Detector* –** The primary objective of this research is to meet the immediate need for an inexpensive, low power, robust trigger to alert inhabitants of an increase in biological aerosol activity, thereby allowing the triggering of more sophisticated systems to determine the identity and source of the pathogen. During 2002 this project resulted in the development and testing of a novel and inexpensive sensor device capable of detecting airborne biological agents. The first three months of the project were dedicated to defining the parameters for sample media such as liquids, aerosols, and solid surfaces. A considerable amount of time was spent in the design and testing phase, as well. The prototype instrument utilizes a recently developed and proven aflatoxin biosensor which utilizes a flashlamp and photomultiplier tube, coupled with miniaturized fluidics to repeatedly sense small amounts of fluorescence in a 2-minute cycle and a high-flow, aerosol concentrator into a single integrated unit. Although there was some experimentation involved in the construction of the detection device, the final test results of the prototype bio-aerosol detector revealed the relationship between the bacterial agents and the intensity of the fluorescence emissions. This prototype device will be improved and refined in 2003 and tests in full-scale building models will be completed.

- ***Development of Near Real-Time Sensors for Chemical Warfare Agents in Indoor Environments -*** The potential use of chemical weapon agents represents a growing global threat and has brought to focus the need for instrumentation that can rapidly detect these compounds at very low levels. The objective of this project is to develop an inexpensive, concealable sensor for monitoring the release of the chemical warfare agents Sarin and Soman in indoor and outdoor environments. Using liquid core waveguide technology and a molecular imprinted polymer designed specifically for recognition of chemical agents, investigators have built a chemical sensor capable of detecting chemical warfare simulants in near real-time. The proof of concept was successful and efforts in 2003 will seek to improve on limiters of detection and timing. Significant leveraging opportunities for this project exist, including the possibility for future collaborations with ITT Industries and the United States Air Force.

Focus Area IV: Building Protection Strategies

- ***Modeling and Simulation of Chemical and Biological Fluid Dispersion within a Building Envelope -*** The Modeling and Simulation (M&S) project has developed an integrated computer model and simulation of the release of chemical and biological agents in urban terrain, including releases within an office building. Along with the ability to predict chemical and biological particle dispersion, these models provide predictions of the relative toxic effects on military and civilian personnel. These simulations should prove useful to the military for training operations designed to test response time for an offensive or terrorist use of chemical and biological weapons. Additional future leverage opportunities exist with both tactical and operational wargaming and virtual battlefield technologies.

Each of these research projects was very successful in meeting its planned objectives and milestones, as well as generating significant information and novel findings to enhance the knowledge base and approaches to countering biological and chemical weapons and threats. Measures of the successes of these research efforts by the Zumwalt Program include the issuance of one patent and two are pending with the U.S. Patent Office, more than 35 peer-reviewed publications are either in print or in press, and 60 professional scientific presentations have been presented in 13 states and five foreign countries as a direct result of this research program to date.

Specific areas of research to be addressed by the Zumwalt Program researchers at Texas Tech during fiscal year 2004 will include:

Focus Area I: Modeling, Simulation and Visualization

- ***Modeling the Transport of Aerosols in the Urban Environment: Real-time Updating of Dispersion Predictions Using Sensor Data -*** Near-real time dispersion codes based on Gaussian Puff and Plume models are essential to the direction of responses to chemical, radiological and biological releases. Aerosol dispersion predictions are currently based on

Second Order Integrated Puff (SCIPUFF) algorithms. One of the major sources of uncertainty in the predictions provided by such codes lies in source characterization. In many cases, it will be difficult or even impossible to directly assess the exact characteristics of a source during the critical early stages of a release, and further uncertainty results from the effects of source location (elevation, position relative to obstacles) on downstream transport. It is sought to develop techniques to integrate sensor data to improve dispersion predictions in real time during the evolution of a release event. It is anticipated that future generations of sensors will provide a spatial concentration field during the evolution of a release event. The proposed research will develop techniques to use this data to develop refined estimates of source characteristics and updated dispersion predictions. The reverse-diffusion problem is inherently ill-posed, eliminating the possibility of direct analytical solution. To address this problem, a neural net algorithm is to be developed to characterize the source from the evolving concentration field. The algorithm will then be applied to evaluate the effect of sensor deployment strategies on the accuracy of, and time taken to achieve, source characterization. The proposed research will be closely integrated with the development of the Texas Emergency Analysis and Response Program (TEARP) operations center. The dispersion modeling tools used in center operations will provide scenarios for use in the evaluation of sensor deployment strategies. The operations center will benefit by using scenario development for both the training of center personnel and the cooperative development of operational strategies with TIPC. The evaluation of sensor deployment strategies provides another opportunity for cooperation with the TEARP center and TIPC, both with regard to strategies for use in emergencies and in the design of permanent sensor arrays to protect key elements of the infrastructure of the State of Texas. As source characterization algorithms are developed, methodologies will be developed to implement the algorithms in conjunction with the Gaussian modeling codes used by TEARP. The algorithms may be tested in an operating environment, and, once successfully validated, implemented for use in emergency operations. Research currently funded enhances understanding of aerosol transport in the urban environment by characterizing the interaction between aerosols and vegetative canopies. While the vast majority of the research effort will be devoted to the research described above, an effort is to be made to pursue elements of the current investigation into the interaction between aerosol species and vegetative canopies to completion. A methodology is to be developed to introduce the local effects associated with vegetation into larger scale Gaussian dispersion models. Further investigation is needed to determine the residence of time of the entering streams within the canopy and the rate at which aerosols entering the canopy can be expected to deposit out on the surfaces of the canopy. These elements may then be combined with previously obtained results to formulate a sink/source term representing vegetation in Gaussian Puff models. An investigation into the effect of wind velocity on the aerodynamic drag force exerted on trees is also to be undertaken in order to establish a framework for adjusting canopy parameters in response to varying wind velocities.

- ***Use of Prognostic Wind Fields and GIS-based Software for Surface-Layer Atmospheric Diffusion Computation -*** This project is a follow-up to the past three years of our work, which has focused on combining meteorological field platform development, mesoscale meteorological models and diffusion modeling technologies to investigate, develop, evaluate the accuracy and effectiveness of, and improve codes simulating the airborne dispersion of chemical/biological agents or other hazardous substances. Past results have indicated that nudging the meteorological models with surface-based data alone appears to have only a limited impact on mesoscale weather and dispersion forecasts: it appears that data from vertical profiles and probes of the atmosphere may be needed for true improvement of model prognostications through data assimilation. A model providing the best tools for evaluation of a dispersing airborne chemical/biological event must provide a balance between complexity, timeliness, and accuracy, and should be able to display results overlain with urban topography in a Geographic Information Systems (GIS) setting. The proposed project will strive to implement these needs, and will represent a partnership with Army Research Laboratory (ARL) scientists. The ARL has been tasked to develop a real-time operational system for short-term weather forecasting for chemical/biological-emergency response applications, and has sought out the expertise of this project's Principal Investigators to assist them towards this goal. This project will include the development of interactive software between the MM5 meteorological model and the CATS-JACE GIS-based software, including the HPAC dispersion model, in order to display airborne dispersion calculations in a GIS environment. A microscale wind model will be developed or acquired, and will be interfaced with the aforementioned dispersion model to provide a fast but sufficiently accurate and detailed windflow prediction in the event of an attack or accidental release. This project utilizes the field facilities of Texas Tech's Wind Science and Engineering Research Center and West Texas Mesonet, leveraged with other ongoing experiments supported by other agencies, to acquire high-resolution surface and upper air wind flow measurements. The MM5 meteorological model will then be "nudged" with these data to determine whether vertical (above-surface) meteorological information improves short-term local forecasting and dispersion calculations and provides a more accurate prediction of the consequences of a chemical/biological release. Finally, a new-generation mesoscale model will begin to be tested to determine whether it can replicate MM5's ability to provide inputs to the HPAC dispersion model. This project will represent an improvement to models of weather and airborne dispersion, supporting the Army's need to rapidly and accurately adjust high-resolution meteorological and dispersion model forecasts to actual observations at a meso (10 to 100 km) scale, as related to the Integrated Meteorological Support System concept. The results of the proposed research will improve the ability not only of the armed forces but also civilian authorities and first responders to use locally-collected weather data to gain a tactical advantage, whether it be on the battlefield or in a civilian emergency.

Focus Area II: Agent Detection, Remediation and Therapeutic Intervention Strategies

- ***Mechanistic Studies of Combinative Toxicity of Biotoxin Mixtures* -** The long-term goal of this research project is to investigate mechanisms of combinative toxic effects of biotoxin mixture(s) on animal and humans and develop prevention strategies against potential use of these mixture(s) as biological warfare threats (BWT) or terrorist attacks. Biotoxins are naturally-occurring toxic agents produced by bacterial, cyanobacteria, fungi, and some species of plants and marine fish, which have caused the tremendous economic loss worldwide and are etiological agents of a variety of animal and human toxicoses. Many biotoxins, such as aflatoxin, T-2 toxin, anatoxin, botulinum toxins, microcystins, ricin, saxitoxin, staphylococcal enterotoxins, and tetrodotoxins, are known to be weaponized or to be available for use as terrorist attack(s). For many years, our research efforts have been only focused on study of single toxin, and a great deal of data regarding individual toxins are well documented. However, little attention has been paid in study of combinative toxic effects of biotoxin mixture(s), which may be more potent and cause more damage to human and animal health. The great challenge currently faced in the field of anti-BWT is how to deal with the attack(s) of toxic biotoxin mixture(s). It is logical to raise the concern because a large quantity of single biotoxin is ready, available for use and our knowledge about the combinative toxicity of toxin mixture(s) is very limited. Therefore, there is an urgent need for understanding the mechanism of combinative toxicity of biotoxin mixture(s), developing rapid and sensitive methods to detect multiple biotoxins in the field and body fluids of animal and humans, and as a long-term shot, developing prevention strategies against possible use of these toxin mixtures. The general hypothesis for this FY04 research proposal is that the combinative toxic effects found in our studies with biotoxin mixtures may be molecularly controlled by the critical gene or gene products for metabolism and detoxification and modulate the process will, to a certain degree, reduce the damage and mortality caused by these toxin mixture(s). The specific aims in this project include: 1) to study molecular mechanisms of combinative acute toxic effects of biotoxin mixtures in rat and fish models. 2) To study molecular mechanisms of combinative cytotoxicity induced by biotoxin mixture in targeted human liver and lung cells. 3) To continue development and validation of rapid and sensitive monoclonal antibodies based method(s) for detecting multiple biotoxins exposures in animals and humans, and 4) To continue screening safe and nontoxic chemicals for detoxifying or antagonizing the combinative acute toxic or cytotoxic effects caused by these toxin mixtures. Biotoxins and their mixtures selected in the project represent most toxins of interest both in the field of anti-BWT and in the scientific community of public health. Through the completion of the proposed study, the mechanisms of combinative acute toxicity and cytotoxicity of selected mixture of biotoxins will be thoroughly explored. The rapid and sensitive method(s) for detecting multiple biotoxins in field and body fluids of animals and humans will be developed and validated. A series of chemicals possessing antagonistic effects against acute toxicity of biotoxin mixture(s) will be identified and studied. This proposal seeks the continuing support from RDECOM for FY2004.The research project titled “Combinative toxicity of biotoxin mixtures” was funded by SBCCOM in FY2001 (DAAD13-00-C-0056), in FY2002 (DAAD13-01-C-0053), and in FY2003 (DAAD13-02-C-0070). The proposed studies for the first two years have been completed and the annual report for each year has been delivered. The delivery arrangement for the FY 2003 will be fully met by the end of this funding year. A large database regarding toxicity and cytotoxicity of individual toxin, combination of two toxin mixtures, and combinations of three toxin mixtures in F344 rats, mosquitofish, human HepG2 and BEAS-2B cells has been set up based on our previous studies. Research proposed will be follow-on from previous research findings with the new specific aims and new methods.

- ***Proteomics and Latent Neurodegeneration Triggered by Warfare Agents: Development of a Novel System for Comprehensive Assessment of Candidate Protein Mediators Using an Array Chip -*** The objective of this proposal is to utilize a protein array chip to develop a novel model system that permits a comprehensive and efficient qualitative assessment of candidate proteins involved in latent neurodegeneration triggered by radiological, biological and chemical warfare agents. The ultimate objective is to identify molecular substrates, define prominent transduction pathways and describe relevant cellular pathophysiology mediating latent neurodegeneration to be able to rationally develop therapeutic interventions that prevent catastrophic life-long neurological problems following exposure to non-lethal amounts of warfare agents by targeting proteins identified as major contributors to neuronal programmed cell death in selected brain regions. Retrospective epidemiological studies document higher incidences of neurodegenerative and other diseases in personnel from the Viet Nam conflict and Gulf War however potential causes and mechanisms are entirely unknown. Chronic neurodegenerative diseases have been mechanistically linked to excitotoxicity, a process that occurs when glutamate abusively activates various glutamate receptors including the AMPA and NMDA subtypes leading to a plethora of intracellular events that are capable of triggering multiple constitutive programmed cell death enzymatic cascades that remain poorly characterized. Moreover, particular cell death mechanisms are likely dependent on many concomitant factors including the physiologic context of the cell and the regional location in the brain. This year we propose to develop a model system using a protein array chip that directly identifies proteins that mediate the pathology of cellular neural degeneration. Protein array technology is a successor to gene micro-array technology and represents an innovative and new, "state-of-the-art" approach that targets many relevant proteins at once and excludes irrelevant proteins by casting a wide net, allowing identification of potential players at the exclusion of others. Proteins are the molecular machinery (work horses) of the cell responsible for all physiologic and pathologic processes. Identification of relevant proteins by traditional methods is particularly problematic since the number of these proteins and enzymatic cascades associated with cell death is rapidly expanding making it impractical to singularly probe each candidate protein. Protein array methodology has the advantage over DNA genomic technology because it directly identifies complexes of proteins that work in molecular ensembles to carry out the pathophysiologic events. Furthermore, this technology translates to more efficient discovery of cellular processes, fostering rapid progression and development of rational therapeutic interventions for field applications. Our major goals/milestones for year 4 continue to be to define potential novel therapeutic approaches that target destructive enzymatic cascades to prevent radiological, chemical or biological warfare agent-induced excitatory neurodegeneration in exposed individuals. The overall intent of our research is to develop a model system to expedite discovery of various proteins that contribute to signal transduction pathways that are common final process responsible for neurotoxicity and neurodegeneration regardless of the nature or type of initiating insult. These studies will identify universal intracellular mediators of neurodegeneration and thereby identify relevant target proteins/enzymes on which to focus development of prophylactic and therapeutic treatments to prevent latent neuropathology in individuals at risk from non-lethal exposures to neurotoxic warfare agents.

- ***Fluorescence based detection of single spores -*** The goal of this project is to combine recent advances in ultraviolet light sources and results of experiments with gated fluorescence detection to prepare a microsystem capable of detection of a single spore. Under past funding from SBCCOM we have developed deep ultraviolet light emitting diodes operating at 280 nm that are an enabling component of new fluorescence-based spore detection systems. We have also developed the microfluidic components using sophisticated electronics needed to realize a practical detection system. The current implementation uses a chelation reaction of terbium with dipicolinic acid (DPA), a unique chemical component of spores, to provide an efficient and long-lived fluorescence signature specific to DPA. This detection method greatly reduces the problem of false positives. The fluorescence efficiency of Tb(DPA)3 is 10,000 times higher than that of native Tb(III). Our current system, based on gated photomultiplier detection, has a sensitivity limit equivalent to 10 spores. This already exceeds the best published results by more than a factor of 70. Higher power LED sources and improvements in the photodetection electronics will reduce the limit of detection to a single spore. The construction and testing of the new system requires an interdisciplinary team of scientists with expertise in Electrical Engineering, Chemistry, and Physics. Such a team, consisting of Profs. H. Temkin (Electrical Engineering), S. Dasgupta (Chemistry), S. Nikishin (Electrical Engineering), and M. Holtz (Physics), has been assembled and proven under the past SBCCOM funding. A simple, compact, and reliable spore detection system would be of great interest to a number of our partners in the Admiral Elmo R. Zumwalt, Jr. National Program for Countermeasures to Biological and Chemical Threats.

- ***Development of Combinatorial Peptides for use in the Detection of and Countermeasures against BWAs -*** Many bioassays and biosensors depend upon antibodies as recognition reagents. While antibodies frequently have the desired sensitivity and selectivity, there can be problems with antibody reagents. In some cases, antibodies may be unobtainable due to the non-antigenic nature of the analyte or the target of interest and need to be analyzed in a sample matrix not compatible with antibody function. This later limitation can be especially important in environmental testing applications, where compounds must be extracted from soil or groundwater with organic solvents. Antibodies are also relatively expensive to produce in large quantities, are susceptible to a variety of environmental agents and conditions, have a relatively short shelf life and require refrigeration or freezing for storage and transport. Recent technology, however, can address these limitations and includes the use of peptides as reagents for sensors. Single -chain peptides are much more robust and have much longer shelf-lives than do more complex proteins such as antibodies. They do not require refrigeration for storage or transport, can be produced in very large quantities inexpensively and are more amenable to a variety of diagnostic and therapeutic formats than are antibodies. For these reasons high affinity, target-specific peptides offer an obvious advantage over the use of antibodies in the detection and/or neutralization of biowarfare agents (BWAs). A program is proposed to develop Phage-Display technology for the isolation and characterization of high affinity peptide ligands which can be used for the identification, simulation, and as countermeasures against of BWAs. For this study, and on the advice of RDECOM, we will target *Y. pestis*, *vaccinia* virus, *B. anthracis* spores botulinum toxin (BoNT) for identification and simulation and cholera toxin (CT) for countermeasure studies.

- ***Counter Terrorism Measures to Combat <u>Yersinia pestis</u> and Cholera Toxin with Selenium Pharmaceuticals -*** Objective: During the last year a selenium-peptide was designed and synthesized that can kill over 3 log units of bacteria (99.9%) in 15 minutes and kill all of the bacteria in 2 hours. This seleno-peptide is specific for only bacteria that express the *Yersinia pestis* F1 antigen on their surface. Thus, the peptide has no effect on other bacteria. This represents the first of a new type of antibiotic that kills by a mechanism for which bacteria cannot develop resistance and that is specific for a single bacterial type. The objective for the next year is to complete the design of this new antibiotic by testing its half-life in vivo. The seleno-peptide will then be modified to extend its half-life and test it on the bacteria in living animals. In addition, we will extend this technology to develop a drug that will inactivate cholera toxin. This will utilize a peptide that was developed by Dr. Joe Fralick on a different SBCCOM project which targets and binds quite well to cholera toxin. Methods: 1. To determine and improve the half-lives of newly selected seleno-peptides and seleno-peptidomimetics in vivo. The peptides will be labeled with tritium and then injected into mice. Half-lives for the existence of the peptide in the blood will then be measured. The same peptides will also be synthesized with attached polyethylene glycol residues to improve their half-life in vivo. 2. To continue to synthesize peptides and peptidomimetic selenium containing compounds that were selected for increased binding to Yersinia pestis and increased stability in vivo. While testing for the half-life in vivo, additional seleno-peptides will be synthesized based upon molecular modeling studies for binding to the F1 protein. These peptides will then be tested by BiaCore binding studies for the ones, which bind best to the F1 protein. 3. To test for the ability of the seleno-peptide or seleno-phage to kill *Y. pestis* in vivo. The best candidates from the half-life studies will be tested for their ability to kill the *Y.pestis* bacteria in vivo. 4. A seleno-peptide that binds to cholera toxin will be synthesized and tested for its ability inactivate the cholera toxin. Significance: This research represents the design and synthesis of a new type of antibiotic that can target a specific bacterial species, and then kill that bacteria by a mechanism for which the bacteria cannot develop a resistance. In addition this same technology, which works extremely well on bacteria, will be extended to the design of a drug that can inactivate a toxin. Both of these new drugs have significance as medical countermeasures for the protection of combat personnel.

Focus Area III: Sensors and Personal Protective Devices

- ***Liquid Crystal Technology Based Diagnostic Sensor for Detecting Nerve Agents -*** Threats of use of Chemical and Biological agents during peace time and warfare have drawn considerable attention. For purposes of countering such threats, it is necessary to detect a variety of synthetic organic chemicals at low concentration levels. Highly sensitive laboratory-based methods of detection (like Gas Chromatography and Liquid Chromatography) for specific chemical compounds do exist. However, these methods are not suited for measurement of personal exposure due to their size, weight and power requirements. Further, many of these techniques require demanding user input for obtaining reliable analytical results. Hence, it becomes imperative that we find an inexpensive, easily-constructed, low weight alternative that requires minimal user input for detecting presence of chemical warfare agents for the protection of personnel in danger of being exposed. To meet this challenge, several approaches have been designed. In the first approach, a pre-treated solid surface presents an array of immobilized chemical receptors that weakly bind LC molecules to orient it in a well-defined direction. Upon exposure, the receptors will selectively bind targeted analytes (driven by competitive H-binding ability) more strongly than they bind the molecules forming the LC. This will release the LC molecules. Since the surface will be pre-treated to define a nanometer-scale topography, the freed LC molecules will be forced to assume a predictable and visually distinct orientation in the absence of receptor-mediated-anchoring of the mesogen at the surface. In the second approach novel liquid crystalline molecules will be designed and synthesized that form LC phase through weakly bonding with each other. These molecules will be placed in an electric/magnetic field which orients the molecules in a well-defined direction. The target molecules, due to their competitive H-bonding ability, will release the LC molecules from each other. This will induce a visually-distinct phase in the liquid crystalline material. This release will also trigger a change in the applied electric field which in turn will be amplified and used for detection. In this approach, the LC molecules will double up as receptors for target analyte molecules. This approach will also allow the flexibility to tuning/designing target specific liquid crystalline molecules. The above will lead to the construction of a detection system that will be sufficiently simple to be easily incorporated into a sensor for personal monitoring. Such a sensor, with low power requirements and production cost will be of diagnostic utility for detecting nerve agents such as Tabun (GA) Sarin (GB) Soman (GD) or VX or their hydrolytic products.

- ***Development of Highly Efficient Nonwoven Chemical Countermeasures Substrates*** - The overall goal of the project is develop nonwoven based chemical countermeasures protective substrates that are multifunctional and highly efficient. Immediate objectives are: 1) to develop "next-to-skin" friendly adsorbent chemical decontamination wipes and liners for chemical protective suits and 2) to develop highly efficient and multifunctional destructive adsorbent nanofiber webs. The proposed project will utilize the “state-of-the-art” H1 needlepunching nonwoven technology to develop a multilayer adsorbent substrate. In addition, a through-air thermal bonding technology will be effectively utilized to develop base substrates with enhanced strength and smoothness. The combined use of the needlepunching and the thermal bonding technologies will result in nonwoven base substrates that have improved mechanical and surface properties. The project will also focus on a new and unexplored territory to develop destructive adsorbent nanofiber webs. These specialized nanowebs will have catalytic degradation action against certain chemical warfare agents and also adsorbency. This multifunctional web will significantly enhance the overall protection and filtration efficiencies of chemical protective substrates. The RDECOM funded chemical protective nonwovens research at TTU has been extremely successful in delivering products on time. A three-layered nonwoven chemical protective substrate has been developed. The chemical protective nonwoven composite substrates were evaluated for their protection and adsorption characteristics at the US Army Natick Soldier Center. Results have been very successful and have shown that the nonwoven composites are good enough to serve as lining materials for JS-LIST chemical protective suits. Overall, the project has tremendous pay-back potential to the US DOD and the society by developing new technologies that enhance the protection efficiencies of currently available chemical countermeasures substrates. The continued support of the RDECOM will help to sustain graduate students to continue their research activities resulting in their intellectual growth and development.

- ***Development of a Field-Deployable, Remotely-Monitored, Area-Wide, Biological Pathogen Detection System -*** Zoonoses, or diseases of wild and domestic animals that can cross over into humans, have shaped history and influenced mankind’s social and cultural behaviors. Many of these naturally-occuring zoonotic pathogens are known to have been weaponized and are classified as potential biological terrorism threat agents. Diseases such as hantavirus, plague (*Yersinia pestis*) and tularemia (*Francisella tularensis*) exist and are maintained in wild rodent and arthropod hosts throughout most of the western United States. These enzootic foci of disease are most often unknown until a human case of disease occurs and field surveillance operations are conducted. Current technologies to identify the reservoirs or vectors of these disease agents involve capture of wild rodents, collection of blood or tissue specimens from the animals, and serological assay, culture growth or polymerase chain reaction methods. These processes and techniques are extremely labor-intensive, expensive and require from days to weeks for definitive results to be obtained. The primary objective of this project is to develop a remotely monitored, near-real time, highly accurate biological agent detection system that can be easily deployed into any environment to detect and report the presence of disease pathogens and infection in a suspect rodent population. The initial step to acquiring our objective will be to develop a molecularly imprinted polymer (MIP) or liquid crystal (LC) absorbance sensor that is sensitive to *Yersinia pseudotuberculosis* (a pathogenic species in rodents very similar to *Y. pestis*). The MIP/LC sensing element will then be integrated into a rodent bait matrix and offered to a rodent known to harbor *Y. pseudotuberculosis*. The fluorescence response signal of the MIP or absorbency response of the LC will be monitored, measured and transmitted to a remote event recorder. Successful development and follow-on enhancement of this biological pathogen detection system will significantly improve public health, preventive medicine and Homeland security response capabilities in the civilian and military environments.

Focus Area IV: Environmental Protection Strategies

- ***Generation and analysis of dust particles potentially containing plant toxins and bacterial spores*** - The objective of this proposal is to identify the relationships between soil materials and the generation of dust particles that contain plant toxins and bacterial spores. Inoculation of soil with a toxic agent would be a simple mechanism to contaminate large military reservations through the dust raised by wind action. The plant-toxin, ricin, and peanut lectin, a non-toxic surrogate for ricin, will be evaluated. The spores of the bacteria *Bacillus cereus*, a surrogate for *Bacillus anthracis*, will initially be evaluated. Characterization of ricin sorption to and desorption from natural and anthropogenic materials has been achieved by our team. Also, the sorption of both ricin and *Bacillus cereus* spores on raw fruits and vegetables has been examined. The potential detachment of dusts containing these toxins or spores has not been evaluated. A local USDA-ARS research facility that examines wind erosion has developed a laboratory apparatus to generate dust particles from soil samples. This technology will be utilized in this research project. A series of experiments to quantify the amount and fraction of dust particles that contain toxins and bacterial spores is to be conducted. Soils are unique materials that are heterogeneous and vary both spatially and temporally. Soils with the same soil texture can exhibit radical differences in dust loss depending on whether the soil is wet or dry. Temperature might also have an effect on dust production. This will be the first year of a multi-year proposal. The relationship between soil properties, dust generation, and wind transport of toxins and spores is complex and cannot be easily or rapidly evaluated.

Leveraging of Successes:

Specific examples of ongoing efforts to leverage the successes and expand the momentum of the Zumwalt Program into additional research areas to address highly vulnerable human health protection and economic stability include: (1) Coordinating the development and establishment of a multidisciplinary project with the Director of Homeland Security for Texas to provide near real-time surveillance, monitoring and predictive modeling of disasters or biological and chemical incidents. (2) Developing and coordinating a multidisciplinary project to provide near real-time surveillance of livestock and field crops for disease indicators to combat agricultural terrorism. (3) Exploiting the successful completion of research and development of a near real-time biological aerosol detector device. (4) Conducted preliminary studies and analysis for the development of multidiscipline, multi-agency projects to quantify and characterize zoonotic diseases classified as potential biological weapon agents occurring in Texas. New research initiatives being pursued as a result of the capabilities, expertise and successes of the Zumwalt Program team include:

- Enhanced sensitivity and specificity of biological and chemical agent sensors.
- Emergency operations support through total visibility and modeling of biological and chemical threats in the environment.
- Active surveillance and monitoring of pre- and post-harvest agricultural production systems.
- Non-woven fabrics technology for protection against and detection of biological and chemical threat agents.
- Adaptation of biological and chemical agent sensor technologies to more directly support homeland security needs.
- Development of integrated medical system/health care surge capacity models to assess biological and chemical terrorism incident response capabilities.
- Expansion of non-wovens materials technology research to improve health and safety of military forces, as well as emergency first responders in diverse environments.
- Design and development of novel approaches to military medical force protection.
- Development of biological and chemical environmental threat recognition, prediction and mitigation technologies.
- Dynamics of zoonotic pathogens and their potential use as biological terror agents.

2. *How does TIEHH work with first responders and state and local government organizations to understand their needs for the technologies being developed at TIEHH? How do you work with them on education, training, and outreach?*

Through the scientific expertise and state-of-the-art technologies available through the collaborations among the Zumwalt Program team members and through leveraging of our successes, an operational capability to augment and supplement emergency response assets in the State of Texas was created. This capability, the Texas Emergency Analysis and Response Program (TEARP), integrates scientific and technical expertise with state-of-the-art computing, communications, information systems, and visualization technologies to create an immediately responsive and highly accurate operational capability to save the lives and protect the property of

Texans during accidental or intentional incidents involving biological, chemical and radiological threat agents.

The TEARP at Texas Tech University is composed of four primary components: (1) A continuous Operations Center which coordinates the gathering and initial assessments of “raw” information, disseminates analyzed information, and maintains communications with supported agencies and services. (2) The Center for Dispersive Processes which utilizes data received from numerous sources to develop predictive plume/cloud/threat dispersion models. (3) Wind Science and Engineering, which utilizes meteorological and other weather information resources to evaluate and predict atmospheric influences at an incident site. (4) Biological and Chemical Threat Assessment, which collects and analyzes epidemiological, epizoological and toxicological data to develop predictive models of biological pathogen threats, chemical hazards and their dispersion. This operational platform will provide Texas law enforcement and emergency response leadership, as well as on-site personnel, the information technologies and capabilities needed to dramatically improve their abilities to safely, effectively and efficiently respond to emergency situations. We are a multidisciplinary team combining scientific and technical expertise, as well as operational experts with an understanding of emergency incident response and support operations. This operational understanding coupled with highly accurate weather and hazardous dispersion prediction technologies will provide on-site emergency responders with what is needed to help save lives and property.

The TEARP will provide a wide variety of technical and relevant information and consultation to on-site authorities and the Governor’s emergency response team through the development and interpretation of predictive models of hazard (plume/cloud) movement in the environment for 1, 2, 3, 6, 12, 24, 48 and 72 hours in the future, thereby ensuring highly accurate, near-real time situational awareness for the Texas SOC and on-site first responders. TEARP utilizes all available US National Weather Service observations, near-real time satellite imagery, and forecast information combined with sophisticated high speed computing capabilities (SGI Super Computer) to provide weather forecasts covering Texas at resolutions ranging from 1-15 km. Additionally, the TEARP can deploy mobile platforms called Vehicular Instrumentation Platform for Emergency Response (VIPER) systems outfitted with biological, chemical, meteorological, and radiological sensors into hazardous areas and environments, to relay near-real time data to decision-makers. The TEARP will maintain a full remote computational backup and satellite distribution network for its products and results to ensure uninterrupted service. Finally, the superior technologies and operational and scientific expertise brought together by the TEARP will make available unprecedented resources to provide training to emergency responders, as well as local and state elected officials, in all aspects of biological, chemical and radiological incident response activities.

Operational Capabilities:

- Deliver rapid, accurate data and predictions to government officials, emergency responders, and emergency/incident site commanders; information to make insightful and knowledgeable decisions.
- Provide real-time dissemination of analysis results through secure communications to prepare for and mitigate an emergent event.

- Continuously deliver accurate, high-resolution, timely weather predictions covering the entire state of Texas.
- Provide state-of-the-art dispersion predictions of pollutants, biological and chemical agents as a result of adverse atmospheric conditions, industrial and transportation accidents, and terrorism-related incidents.
- Provide mobile platforms called Vehicular Instrumentation Platform for Emergency Response (VIPER) systems for deploying biological, chemical, meteorological, and radiological sensors into hazardous areas and environments, to relay near-real time data to decision-makers.
- Ensure dispersion and weather predictions are visualized using leading edge technologies.
- Provide support for local and state emergency response training exercises.
- Provide technical support on the latest in meteorological and particle dispersion modeling and simulation capabilities. Modeling results (complemented with insights and analysis from subject matter experts in biological, chemical, and radiological materials and their relationship to environmental toxicology and epidemiology) will be utilized before, during and after all operational events. These highly accurate assessments will be communicated in user-friendly language to enable use by all facets of governmental infrastructure.
- Maintain a full remote computational backup and satellite distribution network for its products and results to ensure uninterrupted service.

3. *How can the federal government, particularly the Department of Homeland Security, improve its efforts to help communities be better prepared for a bioterrorist attack? Are there specific areas that demand increased attention?*

The following areas require increased attention from the Department of Homeland Security to ensure the American people are protected from the threat of bioterrorism:

1. An increased research focus on the development of more rapid biological pathogen recognition and identification capabilities for use in both active and passive surveillance systems, particularly in areas of high population density.

2. The creation of regionally-focused research laboratories to assess and develop technologies to address the growing threat of emerging and resurging pathogens that may also have the potential for use as biological terror agents, particularly those pathogens specific to or enzootic in geographic regions.

3. An increased focus on the establishment of training and education facilities to provide the most up-to-date information and technologies to emergency responders, their leadership, as well as elected officials, on the preventive and response procedures for biological weapon agents.